

Amendments to the Claims:

This listing of claims will replace all prior versions, and listings of claims in the application.

Listing of Claims:

1 1. (Currently amended) A method of treating a subject with cancer by administration of a
2 macrocyclic metal chelate, said method comprising the steps of:

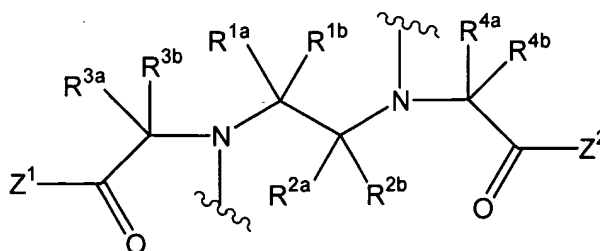
3 (a) administering to said subject an antibody comprising an antigen recognition domain
4 that recognizes said ~~[[a]]~~ macrocyclic metal chelate, wherein said antibody
5 comprises a targeting moiety that binds specifically to a cancer cell by binding
6 with a member selected from a cell surface ~~receptors~~ receptor and cell surface
7 ~~antigens~~ antigen, thereby forming a cell-antibody complex; and

8 (b) administering to said subject said macrocyclic metal chelate, thereby specifically
9 binding said ~~compound~~ macrocyclic metal chelate to said antibody to form a cell-
10 antibody-metal chelate complex.

1 2. (Currently amended) The method of claim 1, wherein said macrocyclic metal chelate
2 comprises four nitrogen atoms.

1 3. (Original) The method of claim 2, wherein at least two of said nitrogen atoms are
2 covalently linked to a substituted or unsubstituted ethyl bridge.

1 4. (Currently amended) The method of claim 2, wherein said macrocyclic metal chelate
2 comprises the subunit:



4 wherein

Z^1 and Z^2 are members independently selected from OR^1 and NR^1R^2 ,

in which

R^1 and R^2 are members independently selected from H, substituted or

unsubstituted alkyl and substituted or unsubstituted heteroalkyl;

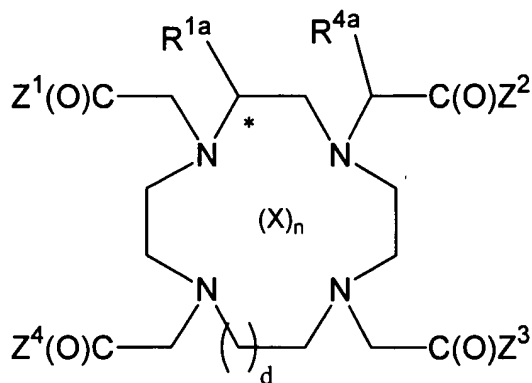
R^{1a} , R^{1b} , R^{2a} , R^{2b} , R^{3a} , R^{3b} , R^{4a} and R^{4b} are members independently selected from

H, substituted or unsubstituted alkyl, substituted or unsubstituted

heteroalkyl, substituted or unsubstituted aryl and linker moieties.

5. (Currently amended) The method of claim 1, wherein said macrocyclic metal chelate is a member selected from substituted or unsubstituted DOTA and substituted or unsubstituted TETA.

6. (Currently amended) The method of claim 4, wherein said macrocyclic metal chelate has the formula:



wherein

R^{1a} and R^{4a} are members independently selected from H, substituted or

unsubstituted alkyl, substituted or unsubstituted heteroalkyl, substituted or unsubstituted aryl and linker moieties;

X is a member selected from a lanthanide, an actinide, an alkaline earth metal, a group IIIb transition metal, and [[or]] a metal;

Z^1 , Z^2 , Z^3 and Z^4 are members independently selected from OR^1 and NR^1R^2

in which

R^1 and R^2 are members independently selected from H, substituted or

unsubstituted alkyl and substituted or unsubstituted heteroalkyl;

- 14 n is a member selected from 0 and [[or]] 1; and
15 d is a member selected from 1 and [[or]] 2.

1 7. (Original) The method of claim 1, wherein said macrocyclic metal chelate comprises a
2 reactive functional group.

1 8. (Currently amended) The method of claim ~~[[5]]~~ 6, wherein the carbon atom marked * is
2 of S configuration.

1 9. (Cancelled)

1 10. (Currently amended) The method of claim 1, wherein said targeting moiety binds
2 specifically ~~to a cell surface protein~~ to said cell surface antigen.

1 11. (Original) The method of claim 1, wherein the targeting moiety is covalently attached to
2 said antibody.

1 12. (Original) The method of claim 10, wherein the targeting moiety is an antibody.

1 13. (Original) The method of claim 11, wherein the targeting moiety specifically binds to a
2 protein on a cancer cell.

1 14. (Original) The method of claim 1, wherein the subject is a mammal.

1 15. (Currently amended) The method of claim ~~[[1]]~~ 14, wherein the mammal is a human.

1 16. (Withdrawn) A method of *in vivo* imaging, said method comprising the steps of:

- 2 (a) administering to a subject an antibody comprising an antigen recognition domain that
3 recognizes a macrocyclic metal chelate, wherein said antibody comprises a
4 recognition moiety that binds specifically to a cell, thereby forming a cell-
5 antibody complex;
6 (c) administering to said subject said metal chelate, thereby specifically binding said
7 compound to said antibody to form a cell-antibody-metal chelate complex; and
8 (d) detecting said cell-antibody-metal chelate complex.

1 17. (Withdrawn) The method of claim 16, wherein said metal chelate comprises four
2 nitrogen atoms.

1 18. (Withdrawn) The method of claim 16, wherein the step of detecting is by positron
2 emission tomography.

1 19. (Withdrawn) The method of claim 16, wherein the step of detecting is by magnetic
2 resonance imaging.

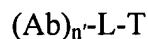
1 20. (Withdrawn) The method of claim 16, wherein the step of detecting is by detection of
2 lanthanide luminescence.

1 21. (Withdrawn) The method of claim 16, further comprising, between steps (a) and (b),
2 administering a clearing agent to said subject.

1 22. (Withdrawn) The method of claim 16, wherein the subject is a mammal.

1 23. (Withdrawn) The method of claim 22, wherein the mammal is a human.

1 24. (Currently amended) The method according to claim 1 wherein said antibody has the
2 structure:



4 wherein,

5 n' is an integer selected from 1 to 10 [[1-10]];

6 Ab represents an antibody comprising an antigen recognition domain that
7 recognizes a macrocyclic metal chelate;

8 L is a member selected from a chemical bond and a [[or]] linking group that may
9 contain one or more functional groups; and

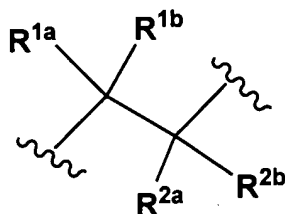
10 T is said targeting moiety.

1 25. (Currently amended) The method of claim 24, wherein said macrocyclic metal chelate
2 comprises four nitrogen atoms.

26. (Previously presented) The method of claim 24, wherein said targeting moiety is an antibody that binds specifically to a cell surface antigen.


27. (Previously presented) The method according to claim 24 wherein said antibody is administered to said subject as a pharmaceutical composition comprising said antibody and a pharmaceutically acceptable carrier.

28. (New) The method according to claim 3, wherein said substituted or unsubstituted ethyl bridge is

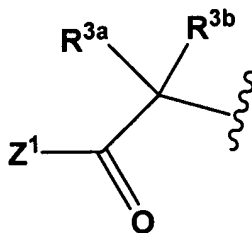


wherein

R^{1a}, R^{1b}, R^{2a} and R^{2b} are members independently selected from H, substituted or unsubstituted alkyl, substituted or unsubstituted heteroalkyl, substituted or unsubstituted aryl and linker moieties.


and wherein each “” indicates the attachment of the ethyl bridge to a nitrogen atom.

29. (New) The method according to claim 2, wherein at least one of said four nitrogen atoms is covalently attached to a structure according to



wherein

Z¹ and Z² are members independently selected from OR¹ and NR¹R²,
in which

16 R^1 and R^2 are members independently selected from H, substituted or
17 unsubstituted alkyl and substituted or unsubstituted heteroalkyl;
18 R^{3a} and R^{3b} are members independently selected from H, substituted or
19 unsubstituted alkyl, substituted or unsubstituted heteroalkyl, substituted or
20 unsubstituted aryl and linker moieties
21 and wherein each “” indicates the site of attachment of the structure to a
22 nitrogen atom.